UNITED STATES DEPARTMENT OF COMMERCE
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DEA/FCE-1994

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/846,996	05/01/97	GREENER A	8142-124-999

18N2/0203

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EXAMINER	
RAILEY, J	
ART UNIT	PAPER NUMBER
1805	5

DATE MAILED: 02/03/98

Please find below a communication from the EXAMINER in charge of this application

Commissioner of Patents

Office Action Summary	Application No. 08/846,996	Applicant(s) Greener et al.
	Examiner J. Railey	Group Art Unit 1805

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-13* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-13* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

The Examiner in charge of, and Art Unit location of, your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1805, Examiner Railey.

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The declaration submitted 23 September 1997 fails to refer to the application by its Serial No. as required in the Notice to File Missing Parts of the Application, form PTO-1533, mailed 10 September 1997. Note item 4. The declaration filed 23 September 1997 only refers to the date of May 1, 1997 and this declaration did not accompany the initial filing papers.

The claims are free of the prior art, as the prior art does not teach a mutated *Hte* region from *E. coli* which can transfer improved competence.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 1 and 2 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to "biologically pure strains" which are defined in the specification at page 5, beginning at line 19 as derived from a single cell. The strain as claimed should be "isolated" to indicate that they are manipulated by the hand

of man. Otherwise, the claims read upon naturally occurring *E. coli*.

Claims 2, 9, 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 has improper Markush-type language. At line 4, the claim should read: "...a buffer comprising at least one **selected from the group consisting of** potassium chloride..."

Claims 12 and 13 provides for the use of cells, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 12 and 13 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). These claims are informal and not in accordance with accepted U.S. practice, as there is no middle ground, such as the "use" of a thing, upon which a claim can rest.

Regarding claim 2, it is unclear what applicant intends by a strain which has been "derived from a strain having the identifying characteristics of ATCC No 55962." It is unclear

how the claimed strain is so derived from a deposited strain. Applicant should claim the strain directly, as having **all** of the identifying characteristics of ATCC No 55962.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the *E. coli* strain deposited as ATCC No 55962 (also called strain XL10-GOLD), as well as methods of preparing other *E. coli* strains having improved competence by P1 transduction from this deposited strain, does not reasonably provide enablement for *E. coli* strains broadly claimed as having an *Hte* mutation or methods of preparing or using gram negative bacteria having improved competence by transfer of an *Hte*$^-$ region. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification teaches the mutagenesis of *E. coli* by treatment with ultraviolet light, followed by screening the surviving cells for increased competency in transformation with plasmid DNA. Four selected strains were then individually subjected to λ::Tn10 mutagenesis to tag essentially all regions of the genome at 1 insertion/100 kilobase pairs of the host chromosome. These Tet^R derivatives are then subjected to P1 lysis, in which 1 % of the packaged

P1 phage contain random 100 kb pieces of host chromosome. The P1 is collected after host cell lysis, and a new round of infection of the packaged P1 phage with a new recipient host is done. These P1 phage may transfer these random fragments, and screening for tetracycline resistance in the new recipient host indicates that this new recipient has acquired the Tet^R gene along with portions of the mutated *E. coli* chromosome of any of the four selected strains. This P1 phage transduction transfers a segment of the host chromosome from the original mutated *E. coli* genome, which will undergo homologous recombination in the recipient to demonstrate that the increased competence phenotype can be transferred to other host cells. If that portion of the *E. coli* genome transferred by P1 phage transduction contains gene segments which improve competence, then repeated rounds of transformation enrichment, screening and selection will prepare isolated transformants which contain the Tet^R transposon inserted adjacent to a segment that provides for improved transformation efficiency, rather than the Tet^R transposon integrated elsewhere. Taking these final transformants and preparing P1 lysates from them will transfer Tet^R to recipient host cells wherein any tetracycline resistant transformants obtained contain the gene segment for improved competence, termed an *Hte* mutation by applicant.

The specification fails to teach the composition of the gene region or regions (called the *Hte* mutation by applicant) from the original mutagenized *E. coli* host cells which results in this increased competence efficiency. Rather, the specification provides that the skilled artisan **might** determine what constitutes this unidentified segment which is transferred by P1 transduction.

The skilled artisan **might** use this segment to transfer to a wide range of gram negative bacteria to improve competency. However, as applicant has not identified the composition of this fragment, it would be impossible for the skilled artisan to make and use the invention as claimed without access to the specific P1 lysate described at page 26, line 20, which was prepared from the isolated transformants after repeated rounds of screening. Applicant has taken transformant #12 as described in the last paragraph at page 26 and used it as a recipient in F' transduction with strain XL2-Blue to generate XL10-Gold, the deposited strain. Presumably, the skilled artisan could perform P1 transduction on XL2-GOLD and obtain the *Hte* segment for transfer to any other strain *E. coli*, and screen for tetracycline resistance and increased competence as given in the specification at page 28, lines 22-29. Consequently, the claims must be limited to the deposited strain or to host *E. coli* strains which are P1 transductants from this deposited strain, and which have this improved competence property. In addition, as it is not disclosed what comprises the *Hte* mutation, it is unclear whether this mutation would function in other gram negative bacteria as broadly claimed. When the *Hte* containing segment is introduced into a given host cell, it must recombine with the corresponding segment found in that host chromosome in order to bring about the improved competence phenotype. As the composition of the gene or genes found on this segment is not disclosed, nor the composition of the corresponding gene or genes in other gram negative bacteria given for comparison, it is unclear whether the instant *Hte* segment would indeed recombine properly in host cells other than *E. coli*.

Applicant's claimed methods must be limited to those in which the polynucleotide sequence from XL2-GOLD is transferred by P1 transduction from the deposited strain into other *E. coli* hosts.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As noted above, the strain XL10-GOLD is required to practice the invention. Claim 2 is particularly drawn to the specific ATCC 55962 deposit of this strain. It is appreciated that the specification at page 7 notes that this deposit has been made in accordance with the Budapest Treaty. However, applicant has not provided a statement that there will be no restrictions placed on its availability upon the issuance of a patent on the instant application serial No. An averment in this regard is required. Note the next-to-last paragraph of the following section:

A declaration by applicant, assignee, or applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection or rejection based on a lack of availability of biological material. See 37 CFR 1.801 through 1.809. Such a declaration:

1. Identifies declarant.

2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address.

3. States that the deposited material has been accorded a specific (recited) accession number.

4. States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent.

5. States that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the

Commissioner to be entitled thereto under 37 C.F.R. 1.14 and 35 U.S.C. § 122.

6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer.

7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) ***and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.***

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Art Unit 1805 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number for Art Unit 1805 is (703) 308-4242 or 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. F. Railey, whose telephone number is (703) 308-0281. The examiner can normally be reached on Monday-Thursday, and alternate Fridays, from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, can be reached at (703) 308-4003. The fax phone number for informal transmissions to the examiner is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

2 February 1998

JOHNNY F. RAILEY II, PH.D.
PRIMARY EXAMINER
GROUP 1800